Bismuth(III) Chloride Catalyzed Efficient and Selective Cleavage of Trityl Ethers[1]

Gowravaram Sabitha,* E. Venkata Reddy, R. Swapna, N. Mallikarjun Reddy, J. S. Yadav

Organic Division I, Indian Institute of Chemical Technology, Hyderabad 500 007, India
Fax +91(40)27160512; E-mail: sabitha@iict.ap.nic.in

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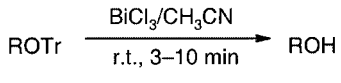
Abstract: A highly selective and efficient protocol has been developed for detritylation using 5 mol% $BiCl_3$ in acetonitrile. The cleavage proceeds at room temperature in high yields and the conditions are mild enough to tolerate a variety of acid-base sensitive functional groups.

Key words: trityl ethers, catalytic, selective, bismuth(III) chloride, alcohols

The triphenylmethyl (trityl) group is a commonly used protecting group for primary alcohols in carbohydrate and nucleoside chemistry due to its ease of installation, removal and stability towards a variety of reagents.[2,3] In general, detritylation is accomplished under strong acidic conditions such as HCOOH,[4] 80% CH_3COOH,[5] mineral acids,[6] CF_3COOH,[7] or using Lewis acids such as $ZnBr_2$,[8] $AlClEt_2$,[9] $Yb(OTf)_3$[10] and $Ce(OTf)_4$.[11] Other reagents including $CeCl_3$/NaI,[12] I_2/MeOH[13] and triethylsilane[14] have also been employed for the removal of trityl group. However, under protic acid conditions, sensitive substrates frequently undergo acid catalyzed deglycosylations, and Lewis acid detritylation procedures require either anhydrous conditions, use of reagents in stoichiometric quantities and extended reaction times and heating. Thus there is still a need to develop a mild and more effective method to overcome the above drawbacks for trityl deprotection. Most bismuth compounds are relatively non-toxic, easy to handle and can tolerate small amounts of moisture. With increasing environmental concerns and the need for 'green reagents', the interest in bismuth and its compounds has increased tremendously in the last decade.[15] In continuation of our studies using $BiCl_3$ for various organic transformations,[16] we report herein a simple, mild and highly efficient method for the cleavage of trityl ethers using a catalytic amount of $BiCl_3$ in acetonitrile at room temperature (Scheme 1).



R = alkyl, aryl, terpenoid and carbohydrate units

Scheme 1

Initially, trityl ether **1a** was subjected to detritylation[17] with 5 mol% of $BiCl_3$ in acetonitrile at room temperature to afford **2a** in 92% yield within 7 minutes. Encouraged by this result, several trityl ethers with different protecting groups were subjected to deprotection using $BiCl_3$ as a mild Lewis acid (Table 1). Thus, trityl ethers **1c** and **1q** containing acid sensitive THP and Boc group respectively underwent facile cleavage of the trityl ether within 4 minutes, retaining the THP and Boc groups. Similarly, trityl ethers **1e**–**h** having base sensitive Ac, Bz, Ts and Piv groups underwent smooth and selective deprotection of the trityl group in 3 minutes to give the corresponding alcohols in good yields. In a further study, sugar substrates possessing glycosidic linkages and *O*-prenyl, *O*-allyl, and Bn groups were also subjected to selective cleavage of trityl groups in 8–10 minutes to afford the corresponding alcohols. The trityl groups of **1d**, **1i** and **1j** were also cleaved without causing loss of the TBDPS and PMB protecting groups. Trityl ethers **1k**–**n** having acetonides derived from secondary alcohols underwent selective deprotection of the trityl group leaving acetonides intact. Whereas, the cleavage of acetonides derived from primary alcohols using $BiCl_3$ is reported.[18] The results show that the rate of detritylation using our conditions is much faster (3–10 min) than those reported in the literature. In addition the selectivity, for cleavage of trityl ethers in the presence of a variety of acid/base sensitive groups and substrates such as carbohydrates, terpenes and amino acids makes this procedure a valuable alternative to the existing procedures.

In conclusion, we have demonstrated that 5 mol% $BiCl_3$ in acetonitrile at room temperature is an effective reagent system for the detritylation. The high yields, speed, and chemoselectivity, render this strategy advantageous and it may find wide application in organic synthesis.

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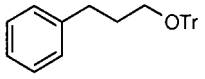
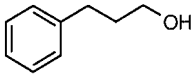
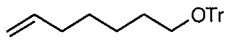
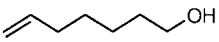
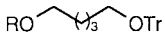
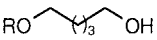
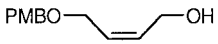
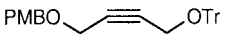
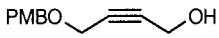
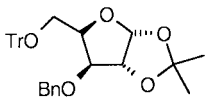
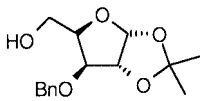
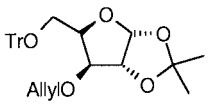
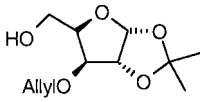
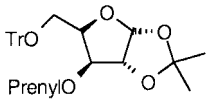
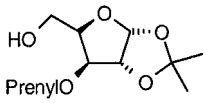
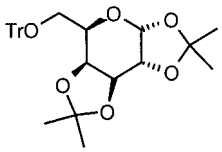
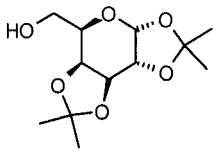
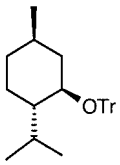
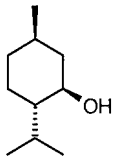
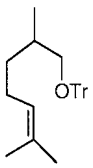
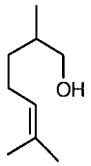
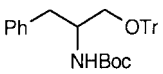
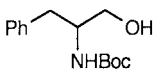
Table 1 $BiCl_3$-Catalyzed Selective Cleavage of Trityl Ethers

Entry	Substrate **1**	Product[a] **2**	Time (min)	Yield (%)[b]
a			7	92
b			6	90
			3	90
c	R = THP	R = THP	4	89
d	R = TBDPS	R = TBDPS	3	93
e	R = Piv	R = Piv	3	95
f	R = Bz	R = Bz	3	92
g	R = Ac	R = Ac	3	88
h	R = Ts	R = Ts	3	86
i			4	90
j			4	90
k			10	95
l			8	90
m			8	92
n			10	95
o			5	92
p			5	93
q			4	90

[a] All products were identified by IR, ^1H NMR, mass spectral data and known compounds by comparison with authentic samples.
[b] Isolated yield after column chromatography.

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(17) **General Procedure.** Trityl ether (2 mmol) in dry MeCN (2 mL), was treated with a catalytic amount of $BiCl_3$ (5 mol%) and stirred at r.t. After complete conversion of the reaction as indicated by TLC, the reaction mixture was filtered through a small pad of Celite. The filtrate was extracted with EtOAc, washed with brine and dried over anhyd Na_2SO_4. After evaporation, the residue was purified by column chromatography using silica gel (60–120 mesh; hexane–EtOAc) to furnish pure alcohol.
Spectroscopic data for selected compounds. Compound **1a**: IR (neat): 2941, 1057, 749 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.92–2.12 (m, 2 H), 2.72 (t, 2 H, *J* = 10.0 Hz), 3.17 (t, 2 H, *J* = 5.1 Hz), 7.12–7.35 (m, 15 H), 7.47 (d, 6 H, *J* = 8.2 Hz). MS: *m/z* = 378 [M^+]. Compound **2a**: IR (neat): 3355, 2943, 1057, 745 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.92–2.12 (m, 2 H), 2.72 (t, 2 H, *J* = 5.2 Hz), 3.63 (t, 2 H, *J* = 9.8 Hz), 7.15–7.25 (m, 5 H). MS: *m/z* = 136 [M^+]. Compound **1d**: IR (neat): 2358, 1219, 1109, 773 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.03 (s, 9 H), 1.38 (s, 2 H), 1.51–1.62 (m, 4 H), 3.02 (t, 2 H, *J* = 5.9 Hz), 3.62 (t, 3 H, *J* = 5.2 Hz), 7.16–7.41 (m, 19 H), 7.39 (d, 6 H, *J* = 7.9 Hz). MS: *m/z* = 585 [M^+]. Compound **2d**: IR (neat): 3332, 2855, 1104, 1028, 772 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.03 (s, 9 H), 1.39–1.59 (m, 6 H), 3.59 (t, 2 H, *J* = 6.0 Hz), 3.64 (t, 2 H, *J* = 6.0 Hz), 7.33–7.38 (m, 2 H), 7.62 (d, 2 H, *J* = 7.3 Hz). MS: *m/z* = 342 [M^+]. Compound **1e**: IR (neat): 2936, 1727, 1156, 1071 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.19 (s, 9 H), 1.46–1.71 (m, 6 H), 3.06 (t, 2 H, *J* = 5.9 Hz), 4.03 (t, 2 H, *J* = 5.9 Hz), 7.18–7.33 (m, 9 H), 7.45 (d, 6 H, *J* = 8.2 Hz). MS: *m/z* = 430 [M^+]. Compound **2e**: IR (neat): 3439, 2938, 1728, 1159, 1057 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.18 (s, 9 H), 1.38–1.72 (m, 6 H), 3.62 (t, 2 H, *J* = 6.6 Hz), 4.04 (t, 2 H, *J* = 6.6 Hz). MS: *m/z* = 188 [M^+]. Compound **1i**: IR (neat): 2361, 1219, 1174, 1060, 771 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 3.60 (d, 2 H, *J* = 6.6 Hz), 3.80 (s, 3 H), 3.85 (d, 2 H, *J* = 6.5 Hz), 4.30 (s, 2 H), 5.60–5.90 (m, 2 H), 6.76 (d, 2 H, *J* = 8.2 Hz), 7.15 (d, 2 H, *J* = 8.1 Hz), 7.30 (m, 9 H), 7.45 (d, 6 H, *J* = 8.2 Hz). MS: *m/z* = 450 [M^+]. Compound **2i**: IR (neat): 3418, 2935, 1514, 1174, 1032 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 3.80 (s, 3 H), 4.01 (d, 2 H, *J* = 6.5 Hz), 4.15 (d, 2 H, *J* = 6.5 Hz), 4.40 (s, 2 H), 5.50–5.90 (m, 2 H), 6.85 (d, 2 H, *J* = 8.2 Hz), 7.27 (d, 2 H, *J* = 8.2 Hz). MS: *m/z* = 208 [M^+]. Compound **1n**: IR (neat): 2985, 2935, 1611, 1509, 1216, 1077 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.31 (s, 6 H), 1.45 (s, 3 H), 1.53 (s, 3 H), 3.50–3.63 (m, 2 H), 3.90 (dt, 1 H, *J* = 6.0 and 2.3 Hz), 4.20–4.30 (m, 2 H), 4.48–4.58 (m, 2 H), 5.50 (d, 1 H, *J* = 5.1 Hz), 7.20 (m, 9 H), 7.40 (d, 6 H, *J* = 7.3 Hz). MS: *m/z* = 503 [M^+]. Compound **2n**: IR (neat): 3425, 2980, 2930, 1509, 1077 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.31 (s, 6 H), 1.45 (s, 3 H), 1.53 (s, 3 H), 3.60–3.73 (m, 2 H), 3.80 (dt, 1 H, *J* = 6.0 and 2.3 Hz), 4.20–4.30 (m, 2 H), 4.48–4.58 (m, 2 H), 5.50 (d, 1 H, *J* = 5.1 Hz). MS: *m/z* = 260 [M^+].
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